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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,472	09/21/2001	Fischetti Vincent	STREPSEQ-1	6764

7590 04/29/2004

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,472	VINCENT ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-275* is/are pending in the application.

4a) Of the above claim(s) *20-52,80-137 and 155-275* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,53-79 and 138-154* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/11/03; 1/11/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-275 are pending in the application.

Election/Restriction

[2] Applicants' election with traverse of the invention of Group I, claims 1-19, 54-79, and 138-154, filed March 19, 2004, is acknowledged. Applicants traverse the restriction requirement by arguing that all of the groups require that class 514, subclass 2 be searched and thus, no additional effort by the examiner is required to perform a search of the listed groups. Applicants' argument is not found persuasive.

In a previous Office action, the examiner acknowledged that Groups I-XI have identical classification (see page 6 of the Office action mailed December 19, 2003.) Although inventions may share identical classification, MPEP 803 states that a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation a different field of search. In a previous Office action, the examiner showed by appropriate explanation that a separate search for each of the inventions is required by stating, "[a]lthough each of inventions I-XI has the same classification, each of the inventions recites unique limitations requiring a separate patent and non-patent literature search and/or sequence search for each Group and thus, co-examination of the inventions of Groups I-XI would place a serious burden on the examiner" (see page 6 of the Office action mailed December 19, 2003.) Applicants do not dispute the examiner's assertion that "each of the inventions recites unique

limitations" and it is the recitation of these unique limitations that results in the requirement of a separate search for each of the inventions. As a separate search is required, co-examination of all claims would place a serious burden on the examiner.

[3] The requirement is still deemed proper and is therefore made FINAL.

[4] It is noted that the examiner improperly included claim 53 in Group IV instead of Group I. In order to clarify the record, it is noted that the correct grouping of the claims of Group I is claims 1-19, 53-79, and 138-154 and the correct grouping of the claims of Group IV is claims 51-52. No other groups were affected by this error.

[5] Claims 20-52, 80-137, and 155-275 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[6] Claims 1-19, 53-79, and 138-154 are being examined on the merits.

Information Disclosure Statement

[7] All references cited in the information disclosure statement (IDS) filed June 11, 2003 have been considered with the exception of references 82 and 83. References 82 and 83 have not been considered as they fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the date of publication is not provided as required by 37 CFR 1.98(b)(5). A copy of the IDS is attached to the instant Office action.

[8] All references of the IDS filed January 11, 2002 that are not duplicates of the references cited in the IDS filed June 11, 2003 have been considered. It is noted that

the cited applications with no corresponding patent number have been lined through in the interest of maintaining confidentiality of unpublished US patent applications.

Oath/Declaration

[9] As stated in a previous Office action, it is noted that the filing dates for application 09/395,636, which applicants' claim domestic priority in the declaration and the first paragraph of the specification, are inconsistent. The declaration indicates a filing date of September 14, 2000 and the first paragraph of the specification indicates a filing date of September 14, 1999. Appropriate correction is required.

[10] As stated in a previous Office action, the oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: The application is objected to because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c). A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

Specification/Informalities

[11] Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The status of nonprovisional parent application 09/846,688 has not been included. It is suggested that applicants insert the expression "now abandoned" following the filing date of this parent application.

Claim Objections

[12] Claims 3, 79, and 143 are objected to in the recitation of "SEQ ID No. 2". 37 CFR 1.821(d) states, "reference must be made to the sequence by use of the sequence identifier, preceded by 'SEQ ID NO:' in the text of the description or claims". It is suggested that, for example, applicants replace "SEQ ID No. 2" with the proper sequence identifier "SEQ ID NO:2".

[13] Claims 10, 69, and 146 are objected to as "nasal drops", "nasal ointments", "nasal washes", and "nasal injections" are recited twice in the claims. Appropriate correction is required.

[14] Claims 58, 63, 76, 140, 145, are objected to because the claims end with two periods. Appropriate correction is required.

[15] Claim 59 is objected to because of the following informalities: the claim does not end with a period. Appropriate correction is required.

[16] Claims 151-153 are objected to under 37 CFR 1.75 as being substantial duplicates of claims 14-15 and 17. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[17] Claim(s) 4-5, 8-16, 19, 53-79, 140-141, and 143 145-152 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 4 (claims 5 and 8 dependent therefrom), 55 (claim 56 dependent therefrom), 63 (claim 64 dependent therefrom), and 140 (claim 141 and 143 dependent therefrom) are confusing in the recitation of "expression system." The art-recognized term for a cellular expression system is a host cell comprising an expression vector encoding a desired protein. It is unclear from claim 4 as to which component of the expression system the "cloning of said transfer vector" occurs. It is suggested that applicants clarify the meaning of the term.

[b] Claim 11 is confusing as depending from claim 8. It appears the claim should depend from claim 9 and has been examined accordingly. It is suggested that applicants clarify the meaning of the claim.

[c] Claims 9 (claims 10 dependent therefrom), 11-16, 60, 68 (claim 69 dependent therefrom), 70-75, 145 (claim 146 dependent therefrom), and 147-152 are confusing in that it is unclear as to where the step of delivering is to be incorporated into

the independent method claims, e.g., where is the step of "delivering said lytic enzyme" as recited in claim 9 meant to be incorporated into the method of claim 1?

[d] Claim 11 is confusing as depending from claim 8. It appears the claim should depend from claim 9 and has been examined accordingly. It is suggested that applicants clarify the meaning of the claim.

[e] Claims 19 and 78 are confusing in the recitation of "[t]he method... ...further comprising an antibiotic". The claims are drawn to methods and not compositions. In the interest of advancing prosecution, the claims have been interpreted as "[t]he method... ...further comprising administering an antibiotic."

[f] Claim 53 (claims 54-60 dependent therefrom) is unclear in the recitation of "treating illnesses or infections of Streptococcus pneumoniae". It is unclear as to whether the term is to be interpreted as treating any illness and infections of Streptococcus pneumoniae or if the term is to be interpreted as treating an illness caused by Streptococcus pneumoniae and treating an infection of Streptococcus pneumoniae. It is suggested that applicants clarify the meaning of the claim.

[g] Claim 61 (claims 62-79 dependent therefrom) is unclear as to where the lytic enzyme is to be administered in step (b). It is suggested that applicants clarify the claim.

[h] Claim 143 is confusing in that there are no bacteria listed therein. It is suggested that applicants clarify the meaning of the claim.

[i] Claim 146 recites the limitation "said carrier". There is insufficient antecedent basis for this limitation in the claim. It appears the claim should depend from

claim 145 rather than claim 138 and in the interest of advancing prosecution, has been examined accordingly.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[18] Claims 1-19, 53-79, and 138-154 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

The claims are drawn to a method for the treatment of Streptococcus pneumoniae by administering a genus of lytic enzymes encoded by a Streptococcus pneumoniae–specific bacteriophage that specifically lyses the Streptococcus pneumoniae cell wall and optionally wherein the genus of lytic enzymes is recombinantly produced from a nucleic acid comprising nucleotides 3687-4577 of SEQ ID NO:2 or a sequence that hybridizes thereto under stringent conditions. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant,

identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. While it is acknowledged that the claims are not drawn to the genus of lytic enzymes themselves, MPEP § 2163 states, "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." In this case, the genus of lytic enzymes and optionally those lytic enzymes encoded by a nucleic acid that hybridizes to nucleotides 3687-4577 of SEQ ID NO:2 is an essential or critical feature that requires adequate description to satisfy 35 USC 112, first paragraph. However, in this case, the specification discloses only a single representative species of the claimed genus of lytic enzymes, i.e., SEQ ID NO:1. The genus of recited lytic enzymes, including those lytic enzymes that hybridize to nucleotides 3687-4577 of SEQ ID NO:2 encompasses species that are WIDELY variant in their structures and functions. As such, the disclosure of the single representative species is insufficient to be representative of the attributes and features of all species as recited in the claimed methods. Given the lack

of description of a representative number of lytic enzymes, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Furthermore, it is noted that the genus of recited lytic enzymes is limited to those that are "coded for" by a bacteriophage or by a Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω-1, and ω–2 bacteriophage. The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997), quoting Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Also, MPEP § 2163 states (citing Amgen, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials". In this case, the specification fails to provide those characteristics that distinguish the subgenus of lytic enzymes "coded for" by a bacteriophage or a Dp-1, Dp-4, Cp-1, Cp-7, Cp-9, Cp-5, MM1, EJ-1, HB-3, HB-623, HB-746, ω-1, and ω–2 bacteriophage from the larger genus of lytic enzymes. For the reasons stated above, the specification fails to provide adequate written description for the recited genus of lytic enzymes.

[19] Claim(s) 1-19, 53-79, and 138-154 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating an S. pneumoniae infection in a mouse nasal cavity comprising administering an effective amount of the polypeptide of SEQ ID NO:1 to a mouse nasal cavity, wherein the polypeptide of SEQ ID NO:1 specifically lyses the cell wall of S. pneumoniae, and optionally wherein SEQ ID NO:1 is recombinantly produced using an E. coli or Bacillus transformant comprising an expression plasmid encoding SEQ ID NO:1 or using a cell-free expression system using an expression plasmid encoding SEQ ID NO:1, does not reasonably provide enablement for a method for treating S. pneumoniae in any organism by administering to any site of infection by any method or those methods as specifically recited in claims 11-16, 70-75, and 147-152 an effective amount of any lytic enzyme encoded by an S. pneumoniae-specific bacteriophage, wherein the lytic enzyme specifically lyses the cell wall of S. pneumoniae and optionally wherein the lytic enzyme is recombinantly produced by any method or by removing and cloning the cognate gene from the phage genome and expressing the gene using an E. coli or Bacillus transformant or a cell-free expression system.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of

predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass a method for treating S. pneumoniae in any organism by administering to any site of infection by any method or those methods as specifically recited in claims 11-16, 70-75, and 147-152 an effective amount of any lytic enzyme encoded by an S. pneumoniae-specific bacteriophage, wherein the lytic enzyme specifically lyses the cell wall of S. pneumoniae and optionally wherein the lytic enzyme is recombinantly by any method or produced by removing and cloning the cognate gene from the phage genome and expressing the gene using an E. coli or Bacillus transformant or a cell-free expression system. In this case the disclosure is limited to a method for treating S. pneumoniae in a mouse nasal cavity comprising administering an effective amount of the polypeptide of SEQ ID NO:1 to a mouse nasal cavity, wherein the polypeptide of SEQ ID NO:1 specifically lyses the cell wall of S. pneumoniae, and optionally wherein SEQ ID NO:1 is recombinantly produced using an E. coli or Bacillus transformant comprising an expression plasmid encoding SEQ ID NO:1 or using a cell-free expression system using an expression plasmid encoding SEQ ID NO:1. While the scope of the claims is overly broad, it should be noted that, based on the wording of the claims, the examiner has

interpreted the claims as meaning only methods of *in vivo* use and not *in vitro* use, for example, disinfecting media comprising a culture of S. pneumoniae.

- The lack of guidance and working examples: The specification provides only a single working example of the claimed method, i.e., the method of treating a mouse nasal S. pneumoniae infection using a Pal polypeptide of SEQ ID NO:1, encoded by nucleotides 3687 to 4577 of SEQ ID NO:2, as set forth at page 27 of the instant specification. This single working example, even in view of the additional teachings of the specification and prior art, fails to provide the necessary guidance for making the entire scope of claimed methods. Other than the enzyme of SEQ ID NO:1, the specification fails to provide guidance regarding other lytic enzymes that are useful for practicing the claimed methods. While it is noted that, at the time of the invention, the polypeptide sequence of the enzyme of SEQ ID NO:1 isolated from Dp-1 was known in the art (see Sheehan et al. Mol Microbiol 25:717-725; cited as reference 129 in the IDS filed June 11, 2003), even if the specification identified other lytic enzymes that are so useful, it is noted that the specification fails to provide sufficient guidance for practicing the full scope of the claims as the specification provides only non-specific, generalized teachings. However, MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application and these generalized teachings fail to provide the necessary specific guidance for practicing the full scope of claimed methods. The specification fails to provide specific teachings for practicing the full scope of the claimed invention, e.g., the composition of the bacteriophage lytic enzyme,

dosages, methods for delivery thereof, areas where administration of the lytic enzyme is likely to be efficacious, and toxicity due to, for example, an immunogenic reaction.

- The high level of unpredictability in the art: There is a high level of unpredictability in practicing the full scope of the claimed methods. It is highly unpredictable as to the lytic enzymes that will be useful for successfully treating S. pneumoniae, including those variants of SEQ ID NO:1 as encompassed by claims 3, 79, and 143, particularly as the specification fails to provide guidance regarding those amino acids of SEQ ID NO:1 that can be altered with an expectation of maintaining the desired therapeutic activity. Moreover, based on the lack of guidance and working examples and the disclosure of only generalized teachings one of skill in the art would recognize the high degree of unpredictability in using this generalized guidance for practicing the full scope of the claimed methods. The degree of unpredictability is compounded further as one must pick and choose from the various routes of administration, compositions, and dosages to arrive at a method that will result in the desired effect.

- The amount of experimentation required is undue: It is NOT routine in the art to identify and screen all lytic enzymes or variants of SEQ ID NO:1 that are useful for practicing the claimed methods. Even if all were identified, it is not routine to attempt all possible combinations of compositions, dosages, routes of administration of the lytic enzyme(s), and sites of S. pneumoniae infection where the lytic enzyme is likely to be efficacious and to screen all possible combinations for toxic effects due to, for example, immunogenicity of the lytic enzyme. Thus, in view of the overly broad scope of the

claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the substantial amount of experimentation, one of skill would recognize that undue experimentation would be necessary for a skilled artisan to make the entire scope of the claimed invention.

As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[20] Applicants' claim to domestic priority under 35 USC 120 and/or 121 to US non-provisional applications 09/846,688, 09/497,495, 09/395,636, and 08/962,523 is

acknowledged. The following art rejections have been raised as the claimed subject matter is not supported by some of the earlier filed applications. In the event the examiner has inadvertently overlooked such support, applicants are invited to direct the examiner's attention to support in the earlier filed applications.

[21] Claim(s) 3-6, 17-18, 63-65, 76-77, 79, 140-143, and 153-154 are rejected under 35 U.S.C. 102(b) as being anticipated by Pelletier et al. (WO 00/32825). It is noted that due to the jumbo size of the cited document, only relevant pages have been provided. The claims are drawn to methods of treating S. pneumoniae by administering a S. pneumoniae bacteriophage specific lytic enzyme produced recombinantly and optionally wherein the lytic enzyme is produced from a nucleic acid comprising nucleotides 3687 to 4577 of SEQ ID NO:2 or a sequence that hybridizes thereto or wherein the bacteriophage is selected from those recited in, e.g., claim 17, or is Dp-1.

Pelletier et al. teach treating S. pneumoniae using a Dp-1 bacteriophage encoded polypeptide (ORF16 as shown at page 371) that is encoded by a nucleic acid that is 100% identical to nucleotides 3687-4577 of SEQ ID NO:2 (pages 22-23; see also Appendix A). Pelletier et al. teach that the nucleic acid encoding the ORF16 polypeptide can be isolated from phage genomic DNA, inserted into a shuttle vector, and introduced into a bacterial host for expression (page 19). This anticipates claims 3-6, 17-18, 63-65, 76-77, 79, 140-143, and 153-154 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[22] Claim(s) 7-8, 58-59, 66-67, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pelletier et al. The claims limit the bacteria for cloning of the transfer vector or limit the expression system to a cell free expression system.

Pelletier et al. disclose the teachings as described in detail above. Pelletier et al. do not teach expressing ORF16 using a E. coli host or using a cell free expression system.

At the time of the invention, it was well known in the art to use E. coli as an expression host as one of ordinary skill in the art recognizes that E. coli are well-characterized and known to express large quantities of a heterologous protein or to use a cell free expression system as one of ordinary skill in the art recognizes that a protein expressed using a cell free expression system is less prone to proteolysis and is easier to purify.

Therefore, it would have been obvious to one of ordinary skill in the art for a method of treating S. pneumoniae using ORF16 expressed by E. coli or using a cell free expression system. One would have been motivated for a method of treating S. pneumoniae using ORF16 expressed by E. coli or using a cell free expression system because of the ease of using E. coli as a host and the expectation of a large yield of

produced protein or because of the ease of purification and reduction in potential proteolysis using a cell free expression system. One would have a reasonable expectation of success for a method of treating S. pneumoniae using ORF16 expressed by E. coli or using a cell free expression system because of the state of art and the results of Pelletier et al. Therefore, claims 7-8, 58-59, 66-67, and 144, drawn to a method of treating S. pneumoniae using ORF16 expressed by E. coli or using a cell free expression system would have been obvious to one of ordinary skill in the art.

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[23] Claims 12-15, 53, 71-74, and 149-152 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 15-17 of US Patent 6,264,945 ('945 Patent). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s)

because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application are drawn to methods for treating S. pneumoniae by parentally administering at least one bacteriophage lytic enzyme, while the claims of the '945 patent are drawn to methods for treating a bacterial infection by parentally administering a lytic enzyme produced by a bacteria infected with a bacteriophage. The claims differ in that the claims of the instant application are limited to treating S. pneumoniae and the lytic enzyme is limited to a bacteriophage-encoded lytic enzyme. The specification of the '945 patent supports an embodiment that would anticipate claims 12-15, 53, 71-74, and 149-152 herein, i.e., the bacterial infection to be treated is S. pneumoniae (see e.g., column 2, lines 25-26) and the lytic enzyme is encoded for by a phage specific for S. pneumoniae (see e.g., column 4, lines 7-11). Claims 12-15, 53, 71-74, and 149-152 of the instant application cannot be considered to be patentably distinct over claims 1 and 15-17 the '945 patent when there is a specifically disclosed embodiment in the '945 Patent that supports claims 1 and 15-17 of the '945 Patent and falls within the scope of claims 12-15, 53, 71-74, and 149-152 herein because it would have been obvious to one of ordinary skill in the art to treat S. pneumoniae by parentally administering a bacteriophage lytic enzyme specific for S. pneumoniae. One of ordinary skill in the art

would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims.

[24] Claims 1, 9-10, 61, 68-69, 138, and 145-146 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 5, 17, 19, 23-27, and 29 of US Patent 6,238,661 ('661 Patent). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application are drawn to methods for treating S. pneumoniae by administering at least one bacteriophage lytic enzyme and optionally delivering the lytic enzyme in a carrier. The claims of the '661 patent are drawn to methods for treating a bacterial infection by administering at least one lytic enzyme produced by a bacteria infected with a bacteriophage. The claims differ in that the claims of the instant application are limited to treating S. pneumoniae and the lytic enzyme is limited to a bacteriophage-encoded lytic enzyme. The specification of the '661 patent supports an embodiment that would anticipate claims 1, 9-10, 61, 68-69, 138, and 145-146 herein, i.e., the bacterial infection to be treated is S. pneumoniae (see e.g., column 3, line 9 and claim 5) and the lytic enzyme is encoded for by a phage specific for S. pneumoniae (see

e.g., column 2, line 66 to column 3, line 2). Claims 1, 9-10, 61, 68-69, 138, and 145-146 of the instant application cannot be considered to be patentably distinct over claims 1-2, 5, 17, 19, 23-27 of the '661 patent when there is a specifically disclosed embodiment in the '661 Patent that supports claims 1-2, 5, 17, 19, 23-27 of the '661 Patent and falls within the scope of claims 1, 9-10, 61, 68-69, 138, and 145-146 herein because it would have been obvious to one of ordinary skill in the art to treat S. pneumoniae by administering a bacteriophage lytic enzyme specific for S. pneumoniae. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims.

[25] Claims 1, 9-10, 19, 61, 68-69, 78, 138, and 145-146, are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 10 of US Patent 6,248,324 ('324 Patent). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application are drawn to methods for treating S. pneumoniae by administering at least one bacteriophage lytic enzyme. The claims of the '324 patent are drawn to methods for treating a dermatological bacterial infection by topically

administering at least one lytic enzyme produced by a bacteria infected with a bacteriophage and a pharmaceutically acceptable carrier. The claims differ in that the claims of the instant application are limited to treating S. pneumoniae and the lytic enzyme is limited to a bacteriophage-encoded lytic enzyme. The specification of the '324 patent supports an embodiment that would anticipate claims 1, 9-10, 19, 61, 68-69, 78, 138, and 145-146 herein, i.e., the bacterial infection to be treated is S. pneumoniae (see e.g., column 3, line 22 and column 4, lines 25-26), the lytic enzyme is encoded for by a phage specific for S. pneumoniae (see e.g., column 2, lines 63-65 and column 3, lines 6-9), and is administered topically (see e.g., column 3, lines 62-66). Claims 1, 9-10, 19, 61, 68-69, 78, 138, and 145-146 of the instant application cannot be considered to be patentably distinct over claims 1-3 and 10 of the '324 patent when there is a specifically disclosed embodiment in the '324 Patent that supports claims 1, 9-10, 19, 61, 68-69, 78, 138, and 145-146 of the '324 Patent and falls within the scope of claims 1, 9-10, 19, 61, 68-69, 78, 138, and 145-146 herein because it would have been obvious to one of ordinary skill in the art to treat an S. pneumoniae dermatological infection by topically administering a bacteriophage lytic enzyme specific for S. pneumoniae using a pharmaceutically acceptable carrier. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims.

[26] Claims 10, 69, and 146 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 44 of US non-provisional application 10/067,979 ('979 Application). An obviousness-

type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application are drawn to (in relevant part) methods for treating S. pneumoniae by administering at least one bacteriophage lytic enzyme by delivering the lytic enzyme in a nasal spray. The claims of the '979 Application are drawn to methods for treating a streptococcal infection by administering a nasal spray comprising a lysine enzyme encoded by a C1 bacteriophage least one lytic enzyme produced by a bacteria infected with a bacteriophage. The claims differ in that the claims of the instant application are limited to treating S. pneumoniae and the lytic enzyme is not limited to a C1 bacteriophage-encoded lytic enzyme. The specification of the '979 application supports an embodiment that would anticipate claims 10, 69, and 146 herein, i.e., the bacterial infection to be treated is S. pneumoniae (see e.g., page 5, bottom of the specification) Claims 10, 69, and 146 of the instant application cannot be considered to be patentably distinct over claim 44 of the '979 Application when there is a specifically disclosed embodiment in the '979 Application that supports claim 44 of the '979 Application and falls within the scope of claims 10, 69, and 146 herein because it would have been obvious to one of ordinary skill in the art to treat S. pneumoniae by

administering a C1 bacteriophage lytic enzyme by nasal spray, wherein the lytic enzyme is specific for S. pneumoniae. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

[27] Status of the claims:

- Claims 1-275 are pending.
- Claims 20-52, 80-137, and 155-275 are withdrawn from further consideration.
- Claims 1-19, 53-79, and 138-154 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

04-28-04

APPENDIX A

```
RESULT 1
AAA69184
ID   AAA69184 standard; DNA; 891 BP.
XX
AC   AAA69184;
XX
DT   27-OCT-2000  (first entry)
XX
DE   Bacteriophage Dp-1 nucleotide sequence dp1ORF016.
XX
KW   Bacteriophage; antimicrobial; genome; identification; antibacterial;
KW   bacterial growth inhibition; bacterial infection; ds.
XX
OS   Bacteriophage Dp-1.
XX
PN   WO200032825-A2.
XX
PD   08-JUN-2000.
XX
PF   03-DEC-1999;   99WO-IB002040.
XX
PR   03-DEC-1998;   98US-0110992P.
PR   03-JUN-1999;   99US-00326144.
PR   28-SEP-1999;   99US-00407804.
PR   30-SEP-1999;   99US-0157218P.
PR   01-DEC-1999;   99US-0168777P.
PR   02-DEC-1999;   99US-00454252.
XX
PA   (PHAG-) PHAGETECH INC.
XX
PI   Pelletier J,  Gros P,  Dubow M;
XX
DR   WPI; 2000-412361/35.
DR   P-PSDB; AAB16697.
XX
PT   Identifying a bacteriophage coding region for treating bacterial
PT   infections comprises identifying a nucleic acid encoding a product that
PT   inhibits bacteria when a bacteriophage infects a bacterium.
XX
PS   Example 17; Page 371; 456pp; English.
XX
CC   The present invention describes a method for identifying a bacteriophage
CC   coding region encoding a product active on an essential bacterial target.
CC   The method comprises identifying a nucleic acid sequence encoding a gene
CC   product that provides a bacteria-inhibiting function when an
CC   uncharacterised bacteriophage infects a pathogenic bacterium. The
CC   compound active on a target of a bacteriophage inhibitor protein in a
CC   bacteria is used to treat or prevent a bacterial infection in an animal.
CC   AAA68243 to AAA69442 and AAB16523 to AAB16954 represent bacteriophage
CC   nucleotide and protein sequences which are used in the exemplification of
CC   the present invention
XX
SQ   Sequence 891 BP; 248 A; 185 C; 231 G; 227 T; 0 U; 0 Other;

  Query Match             100.0%;  Score 891;  DB 3;  Length 891;
  Best Local Similarity   100.0%;  Pred. No. 1.6e-288;
  Matches  891;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ATGGGAGTCGATATTGAAAAAGGCGTTGCGTGGATGCAGGCCCGAAAGGGTCGAGTATCT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGGGAGTCGATATTGAAAAAGGCGTTGCGTGGATGCAGGCCCGAAAGGGTCGAGTATCT 60

Qy         61 TATAGCATGGACTTTCGAGACGGTCCTGATAGCTATGACTGCTCAAGTTCTATGTACTAT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TATAGCATGGACTTTCGAGACGGTCCTGATAGCTATGACTGCTCAAGTTCTATGTACTAT 120
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Qy      121 GCTCTCCGCTCAGCCGGAGCTTCAAGTGCTGGATGGGCAGTCAATACTGAGTACATGCAC 180
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Db      121 GCTCTCCGCTCAGCCGGAGCTTCAAGTGCTGGATGGGCAGTCAATACTGAGTACATGCAC 180

Qy      181 GCATGGCTTATTGAAAACGGTTATGAACTAATTAGTGAAAATGCTCCGTGGGATGCTAAA 240
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Db      181 GCATGGCTTATTGAAAACGGTTATGAACTAATTAGTGAAAATGCTCCGTGGGATGCTAAA 240

Qy      241 CGAGGCGACATCTTCATCTGGGGACGCAAAGGTGCTAGCGCAGGCGCTGGAGGTCATACA 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy      301 GGGATGTTCATTGACAGTGATAACATCATTCACTGCAACTACGCCTACGACGGAATTTCC 360
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Qy      361 GTCAACGACCACGATGAGCGTTGGTACTATGCAGGTCAACCTTACTACTACGTCTATCGC 420
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Qy      421 TTGACTAACGCAAATGCTCAACCGGCTGAGAAGAAACTTGGCTGGCAGAAAGATGCTACT 480
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Qy      481 GGTTTCTGGTACGCTCGAGCAAACGGAACTTATCCAAAAGATGAGTTCGAGTATATCGAA 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy      541 GAAAACAAGTCTTGGTTCTACTTTGACGACCAAGGCTACATGCTCGCTGAGAAATGGTTG 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy      601 AAACATACTGATGGAAATTGGTATTGGTTCGACCGTGACGGATACATGGCTACGTCATGG 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 AAACATACTGATGGAAATTGGTATTGGTTCGACCGTGACGGATACATGGCTACGTCATGG 660

Qy      661 AAACGGATTGGCGAGTCATGGTACTACTTCAATCGCGATGGTTCAATGGTAACCGGTTGG 720
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Db      661 AAACGGATTGGCGAGTCATGGTACTACTTCAATCGCGATGGTTCAATGGTAACCGGTTGG 720

Qy      721 ATTAAGTATTACGATAATTGGTATTATTGTGATGCTACCAACGGCGACATGAAATCGAAT 780
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Qy      781 GCGTTTATCCGTTATAACGACGGCTGGTATCTACTATTACCGGACGGACGTCTGGCAGAT 840
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Db      781 GCGTTTATCCGTTATAACGACGGCTGGTATCTACTATTACCGGACGGACGTCTGGCAGAT 840

Qy      841 AAACCTCAATTCACCGTAGAGCCGGACGGGCTCATTACTGCTAAAGTTTAA 891
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Db      841 AAACCTCAATTCACCGTAGAGCCGGACGGGCTCATTACTGCTAAAGTTTAA 891
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